

In the claims

Please amend claims 1-6, 18-19, and 22-23 as follows:

- Sub B1*
1. (AMENDED) A method of performing high throughput mass spectrometry screening, the method comprising:
- (i) growing one or more cell in vitro;
 - (ii) purifying a sample containing one or more non-column-separated component from the one or more cell, the purifying comprising an off-line parallel purification system;
 - (iii) injecting the sample containing one or more non-column-separated component into a mass spectrometer, wherein the non-column-separated component has not undergone prior separation on a chromatography column; and,
 - (iv) performing flow-injection analysis using electrospray tandem mass spectrometry on the one or more non-column-separated component from the one or more cell, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more non-column-separated component.
- A2*
2. (AMENDED) The method of claim 1, wherein step (i) occurs simultaneously with step (ii), and wherein said one or more cell is alive during step (ii).
3. (AMENDED) The method of claims 1 or 2, wherein at least about 100 cell colonies are screened for presence of the one or more non-column-separated component in less than an hour.
4. (AMENDED) The method of claim 1, wherein at least about 200 cell colonies are screened for presence of the one or more non-column-separated component in less than an hour.

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5. (AMENDED) The method of claim 1, wherein at least about 500 cell colonies are screened for presence of the one or more non-column-separated component in less than an hour.

6. (AMENDED) The method of claim 1, wherein at least about 1000 cell colonies are screened for the presence of the one or more non-column-separated component in about 1 day.

18. (AMENDED) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) growing one or more cell in vitro;
(ii) purifying a sample containing one or more non-column-separated component from the one or more cell,

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wherein the purifying comprises attaching the one or more non-column separated component to a solid support in an off-line parallel purification system, and

wherein the solid support comprises one or more magnetic beads, one or more agarose beads, one or more polystyrene beads, one or more pins, a microwell plate, or a membrane;

(iii) injecting the sample containing the one or more non-column-separated component into a mass spectrometer, wherein the non-column-separated component has not undergone prior separation on a chromatography column; and,

(iv) performing flow-injection analysis using electrospray tandem mass spectrometry on the one or more non-column-separated component from the one or more cell, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more non-column-separated component.

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19. (AMENDED) The method of claim 18, wherein the one or more non-separated column component comprises a library of enzymes, which enzymes each comprises a tag moiety, and wherein the solid support comprises a tag binding moiety.

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22. (AMENDED) The method of claim 18, wherein the one or more non-column-separated component comprises one or more enzyme substrate and one or more product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the one or more product of an enzyme reaction and the one or more enzyme substrate.

23. (AMENDED) The method of claim 18, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing a method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry.

In accordance with the requirements of 37 C.F.R. § 1.121, a marked up version showing the changes to the claims is attached herewith as Appendix A.

Please add new claims 72-80 as follows:

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72. (NEW) centrifugation of cells.

The method of claim 1, wherein purifying comprises

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73. (NEW) cells.

The method of claim 1, wherein purifying comprises filtration of

Sub B1

74. (NEW) The method of claim 5, wherein the off-line parallel purification system comprises an ion exchange resin.

75. (NEW) The method of claim 1, wherein the off-line parallel purification system comprises the addition of an organic solvent to the sample.

76. (NEW) The method of claim 1, wherein the off-line parallel purification system comprises solid phase extraction.

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77. (NEW) The method of claim 1, wherein an automatic sampler transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis at a rate of at least 100 samples or more an hour.

78. (NEW) The method of claim 1, wherein 5 to 100 samples are pooled before performing flow-injection analysis using electrospray tandem mass spectrometry.

79. (NEW) The method of claim 1, wherein the one or more non-column-separated component comprises one or more enzyme substrate and one or more product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the one or more product of an enzyme reaction and the one or more enzyme substrate.

80. (NEW) The method of claim 1, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing a method selected from the group consisting of neutral loss mass spectrometry and parent ion mass spectrometry.